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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/248,964	02/12/1999	KAI W. WUCHERPFENNIG	HAR-005	9407

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EXAMINER	
DECLOUX, AMY M	
ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/248,964	Applicant(s) WUCHERPFENNIG ET AL.	
	Examin r Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 114-133* is/are pending in the application.

4a) Of the above claim(s) *1-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *114-133* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment, drawings and declaration filed 1-31-02 (Papers 23, 22 and 21, respectively) are acknowledged and have been entered.

In view of said applicant's amendment and declaration, all outstanding rejections have been withdrawn.

However, in view of the newly added claims, a new grounds rejection has been imposed.

Formal drawings and/or photographs, filed 1-31-02, fail to comply with 37 CFR 1.84. Please see the attached PTO-948 form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A). Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B) Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 125-128 and 131-133 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 125-127 are not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of " An MHC Class II fusion protein comprising a heterodimer , wherein the first polypeptide comprises a fusion of an extracellular domain of an MHC Class II alpha chain and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of an extracellular domain of an MHC Class II beta chain and a second coiled-coil dimerization domain; wherein said fusion protein further comprises a first immunoglobulin fc domain positioned at the C terminus of one of the first and second polypeptide chains".

Claim 128 is not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of "An MHC Class II fusion protein comprising a heterodimer , wherein the first polypeptide

comprises a fusion of an extracellular domain of an MHC Class II alpha chain and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of an extracellular domain of an MHC Class II beta chain and a second coiled-coil dimerization domain; wherein said fusion protein further comprises a first flexible molecular linker covalently linking the MHC class II alpha chain to the first dimerization domain and a second flexible molecular linker covalently linking the MHC class II beta chain to the second dimerization domain".

Claims 131-133 are not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of " A MHC Class II-peptide complex comprising at least one Class II MHC fusion protein comprising a heterodimer ...., wherein the first polypeptide comprises a fusion of..... an extracellular domain of an MHC Class II alpha chain and ....a flexible molecular linker, and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of .....an extracellular domain of an MHC Class II beta chain and.... a flexible molecular linker, a second coiled-coil dimerization domain; wherein an fc domain is covalently attached to the C' terminus of one of the first and second dimerization domains... and an MHC binding peptide covalently bound to the MHC Class II fusion protein". It is noted that claims132 and 133 are being examined as if they depend on claim 131. Clarification is required by applicant.

There is no written description of the claimed invention in the specification or claims as originally filed. Thus the claimed invention constitutes **new matter.**

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 114, 125-127 and 131-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 114 is indefinite in the recitation in line 2 of the phrase "comprises 5-180 of an MHC Class II α chain" because the meaning of said phrase is unclear. Inserting the word "residues" after the word "comprises" is one way to overcome the rejection.

b. Claims 125-127 are indefinite in the recitation in line 2 of claim 125 of the phrase "one of the first and second" because the meaning is not clear. Substituting the word "or" for the word "and" is one way to overcome the rejection.

c. Claims 131-133 are indefinite in the recitation in lines 11-12 of claim 131 of the phrase "one of the first and second" because the meaning is not clear. Substituting the word "or" for the word "and" is one way to overcome the rejection.

d. Claim 131 is indefinite in the recitation in line 15 of the phrase "the MHC Class II fusion protein" because the claim encompasses two fusion proteins and it is not clear which fusion protein is being referred to.

e. Claim 132 is indefinite in the recitation in line 1 of the phrase "of claim 132" because a claim can not depend on itself. For examination purposes only

the phrase "of claim 132' has been substituted by the phrase "of claim 131". Applicant is required to clarify.

f. Claim 133 is indefinite in the recitation in line 1 of the phrase "of claim 132 claim 132" because the meaning is not clear. For examination purposes only the phrase "of claim 132 claim 132" has been substituted by the phrase "of claim 131". Applicant is required to clarify.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 103, 122-123 and 129 are rejected under 35 U.S.C. 102(a) as being anticipated by Scott et al. J. Exp. Medicine 183:2087-2095 (May 1996), as evidenced by US patent 5,837,816.

Scott et al teach a Class II MHC fusion protein comprising a heterodimer , wherein the first polypeptide comprises a fusion of an extracellular domain of an MHC Class II alpha chain and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of an extracellular domain of an MHC Class II beta chain and a second coiled-coil dimerization domain, as recited in claim 103, (see entire article, especially the Summary). Said fusion protein taught by Scott et al comprises a leucine zipper domain as recited by claim 122, (see entire article, especially the Summary). Scott et al also teaches said fusion protein further comprising an MHC

binding peptide, wherein said peptide is bound to the MHC Class II fusion protein, as recited in claim 129 (see entire article, including page 2091) .

Claim 123 is included because '816 teaches that a leucine zipper refers to a repetitive heptad motif containing 4-5 leucine residues (see entire patent including column 1, lines 55-60). Therefore the referenced teachings anticipate the claimed invention.

7. Claims 114-115 and 118-119 are rejected under 35 U.S.C. 102(a) as being anticipated by Scott et al. as applied to claims 103 etc above, as evidenced by Kalandadze Journal of Biological Chemistry 271:20156-20162 (1996).

Scott et al teach as above. Scott et al does not teach that the referenced MHC fusion protein comprises residues 5-180 or residues 5-200 of an MHC Class II alpha chain as recited in claims 114-115. Nor does Scott et al specifically teach that the referenced MHC fusion protein comprises residues 5-185 or residues 5-205 of an MHC Class II beta chain as recited in claims 118-119. However, Scott et al teach on page 2089, column 1, that the MHC Class II molecules were truncated at the transmembrane region. Kalandadze et al teaches the extracellular domain of DR-alpha consists of residues 1-191, and that the DR-beta extracellular domain consists of residues 1-198. Therefore the referenced teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 116-117 and 120-121 are rejected under 35 U.S.C. 103(a) as being obvious over Scott et al.

Scott et al teach as above. Scott et al does not teach that teach that the referenced MHC fusion protein comprises an MHC Class II alpha chain that is an HLA-DR2 allele, or DRA*0101 or DRA*0102, nor that it comprises an MHC Class II beta chain that is an HLA-DR2 allele, or DRB1*01, DRB1*15, DRB1*16 or DRB1*01. However Scott et al teaches that IA molecules are the murine equivalent of human HLA-DQ and HLA-DR molecules (see entire article including page 2087, column 1).

Scott et al also teaches that said fusion proteins can be used for crystallization as well as for activation of T cells and measurement of MHC Class II-TCR interactions (see entire article, especially the Abstract).

Therefore, one of skill in the art who wanted to study TCR-MHC Class II interactions with the ultimate goal of treating T cell mediated diseases in humans, would have been motivated to produce human soluble class II fusion proteins by using the methodology taught by Scott et al in making the murine soluble class II fusion proteins because Scott et al teaches that IA molecules are the murine equivalent of human HLA-DQ and HLA-DR molecules, and therefore would have had a reasonable expectation of success. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. Claim 124 is rejected under 35 U.S.C. 103(a) as being obvious over Scott et al. as applied to claims 103 etc above in view of US Patent No. 5,837,816.

Scott et al teach as above. Scott et al does not teach that the leucine zipper domain is selected from the group consisting of a Fos and a Jun leucine zipper domain.

'816 teaches that fos and jun comprise leucine zipper domains which preferentially form a heterodimer (see entire patent, especially column 4, lines 44-50).

Therefore, one of skill in the art who wanted to study TCR-MHC Class II interactions with the ultimate goal of treating T cell mediated diseases in humans, would have been motivated to produce human soluble class II fusion proteins comprising a Fos and a Jun leucine zipper domain because fos and jun comprise

leucine zipper domains which preferentially form a heterodimer, and therefore one would have a reasonable expectation of success in forming a soluble MHC Class II heterodimer . Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claim 130 is rejected under 35 U.S.C. 103(a) as being obvious over Scott et al. as applied to claims 103 etc above in view of US Patent No. 6,015,884.

Scott et al teach as above. Scott et al does not teach that the MHC binding peptide is covalently bound to the MHC class II fusion protein.

'884 teaches that an MHC peptide is covalently linked to a soluble Class II heterodimer (see entire patent, especially Figure 1C) and that said heterodimer has potential use as an immune modulating agent (see entire patent, especially column 5, lines 29-32).

Therefore, one of skill in the art who wanted to treat T cell mediated diseases in humans, would have been motivated to produce soluble class II heterodimeric fusion proteins comprising a MHC binding peptide is covalently bound to the MHC class II fusion protein, because one would have a reasonable expectation that said covalently linked peptide would most likely to bind the Class II heterodimer, given its proximity to the Class II binding cleft, and therefore would be effective as modulating agent. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. This application contains claims1-20 drawn to an invention nonelected with traverse in Paper No. 17, filed 5-7-01. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers

for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644

Amy DeCloux, PhD
Patent Examiner, 1644
May 6, 2002